

Takayasu's disease

A report of 3 cases

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Summary

Three patients with Takayasu's disease are described. In 2 cases aortography demonstrated an occlusion of the great vessels at the origin of the arch of the aorta. In 1 patient there was concomitant aneurysmal dilatation of the brachiocephalic trunk. Common and internal carotid artery stenosis occurred in 1 patient and was associated with hemiplegia and blindness. All 3 patients had constitutional symptoms and signs of the disease as well as markedly elevated erythrocyte sedimentation rates; 2 patients had moderate clinical responses to steroid administration in the short term and 1 developed bilateral calf vein thrombosis, which responded satisfactorily to conservative management.

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(ESR) 120 mm/1st h (Westergren). The left radial pulse was markedly weaker than the right with typical vasospasm of the left hand. Besides a weak radial pulse and positive pallor test with elevation of the hand there were no trophic signs. Retinal examination revealed a central scotoma.

Collagen screening tests and serological tests for syphilis were negative. She was not a diabetic and the lipid profile was normal. Protein electrophoresis showed elevated γ -globulin and α_2 -globulin values.

Duplex Doppler ultrasound investigation demonstrated a markedly stenotic origin of the left common carotid and subclavian artery complicated by aneurysmal dilatation of the right brachiocephalic trunk. These findings were confirmed by arteriography of the aortic arch (Figs 1 and 2).

At first prednisone 60 mg/kg/d was given and after 3 months this was reduced to 10 mg/kg/d. The ESR decreased from 120 to 30 mm/1st h (Westergren) but the frequency and manifestations of vasospasm remained unchanged. Visual disturbance stabilized but the decreased left radial pulse pressure remained unchanged.

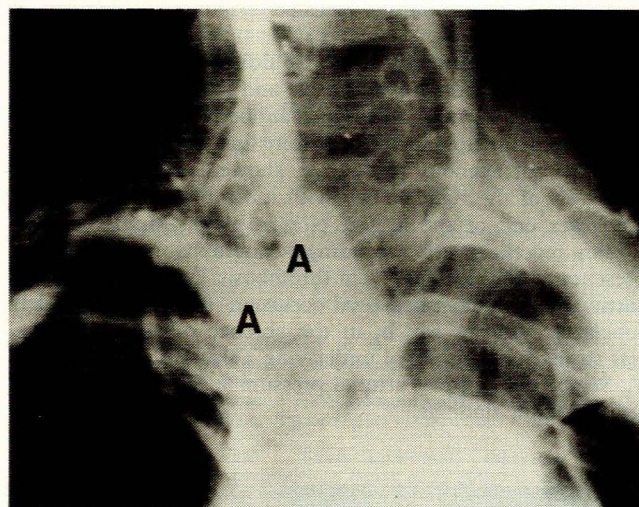


Fig. 1. Case 1. Arch aortogram showing aneurysmal dilatation of the right brachiocephalic trunk with involvement of the orifices of the subclavian and common carotid arteries (A = aneurysm).

In 1908 Takayasu, a Japanese ophthalmologist, published a report of the curious fundal appearance in a 21-year-old woman.¹ He focused attention on a clinical syndrome, which had been described under a plethora of names, characterized by ocular disturbance and weakening or absent upper extremity pulses caused by narrowing or obliteration at the origin of the great vessels arising from the aortic arch.²⁻⁷ The term pulseless disease was suggested by Shimizu and Sano⁸ in 1951. Although the disease is prevalent in Asia, it is encountered throughout the world and a number of well-documented cases have been reported from Japan, Korea and South Africa.⁹

The symptoms, signs and treatment of 3 patients with Takayasu's disease are discussed.

Case reports

Case 1

A 23-year-old coloured woman presented with a 4-month history of malaise, visual disturbance of the left eye of recent onset and manifestations of Raynaud's phenomenon of the left hand.

Clinical examination revealed a right brachial artery blood pressure of 160/90 mmHg, pulse rate 88/min, haemoglobin concentration 9,5 g/dl, and erythrocyte sedimentation rate

Case 2

A 30-year-old coloured woman presented with a 4-month history of anorexia, weight loss, fever, dizziness, frontal headaches and a maculopapular skin rash. She was a moderate smoker and had 5 children.

On examination she was anaemic and appeared chronically ill with signs of recent weight loss. The blood pressure was not recordable in the arms, and the brachial and radial pulses were absent bilaterally. The haemoglobin concentration was 7,8 g/dl, leucocyte count $12,9 \times 10^9/l$ and ESR 130 mm/1st h (Westergren). Cardiovascular examination revealed cardiovascularly associated with a soft pansystolic murmur maximally

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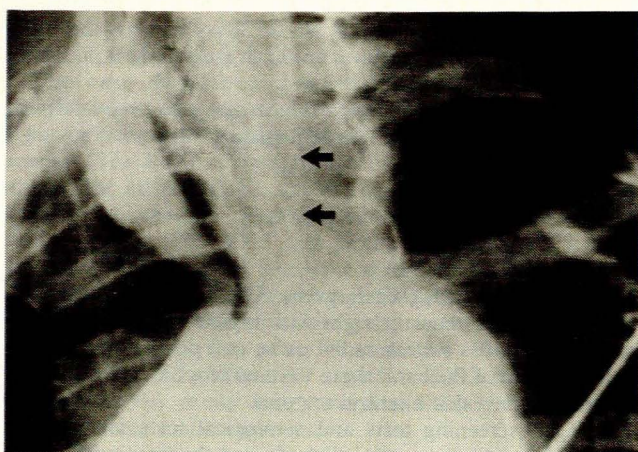


Fig. 2. Case 1. Arch aortogram showing obliteration of the origin of the left common carotid artery (arrows).

audible over the mitral area. Respiratory examination revealed bilateral rhonchi. The foot pulses were present together with moderate calf swelling and tenderness of the left leg suggesting calf vein thrombosis.

Special investigations elicited a hypochromic normocytic anaemia. Serum glucose and creatinine values were normal and serological screening for syphilis was negative. A purified protein derivative (PPD) (tuberculin) skin test was negative. Three sputum investigations for acid-fast bacilli were negative. Liver function tests showed elevated alkaline phosphatase and α_2 -globulin levels.

Fluorescent antibody tests including antinuclear, anti-mitochondrial, anti-smooth muscle and anti-parietal cell tests were negative. Thyroid microsomal antibody haemagglutination tests and rheumatoid factor determination were non-contributory. An intravenous pyelogram showed moderate hydronephrosis of the right kidney with incomplete obstruction at the lower end of the ureter. Non-invasive Doppler venous studies together with ascending venography confirmed the presence of left-sided calf vein thrombosis. Aortography of the aortic arch demonstrated total occlusion of the right and left subclavian arteries which, in the absence of atherosclerosis, was strongly suggestive of underlying Takayasu's disease (Fig. 3). Segmental Doppler arterial pressure studies confirmed the arteriographic findings.

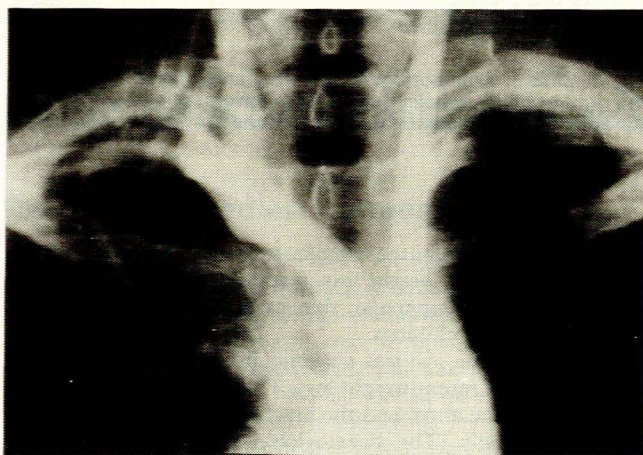


Fig. 3. Case 2. Arch aortogram showing occlusion of the right and left subclavian arteries.

The patient was treated with prednisone 60 mg/kg/d, elevation of the left leg and anti-inflammatory agents for deep-vein thrombosis. Within 10 days the calf swelling and tenderness rapidly improved. One month later prednisone was reduced to 10 mg/kg/d. She was readmitted to hospital 1 month later because of calf vein thrombosis of the right leg. On this admission the ESR was 70 mm/1st h (Westergren). Intravenous heparin combined with coumadin treatment was not administered in this case. The reduced ESR was associated with improvement in her general condition.

Case 3

A 28-year-old white woman was admitted to hospital 2 months after she had first been seen with an acute onset of right hemiparesis and partial blindness of the left eye. She had a past history of primary infertility and suffered from migraine, malaise, and intermittent pyrexia of unknown origin.

On examination her blood pressure was 140/110 mmHg, pulse rate 96/min and haemoglobin concentration 10.5 g/dl. Neurological examination revealed a right-sided hemiparesis and motor dysphasia. Pulses were present in both arms but reduced in volume. The left common carotid artery pulse was markedly reduced and a soft bruit was audible over the carotid bifurcation.

Special investigations revealed a leucocyte count of $10.0 \times 10^9/l$, ESR 110 mm/1st h (Westergren), normal blood glucose level, negative serological tests for syphilis and collagen disease and a normal lipogram. As in the previous 2 cases liver function tests showed elevated α_2 -globulin values. A PPD skin test and cerebrospinal fluid on lumbar puncture were normal. An oral glucose tolerance test was within normal limits.

Computed tomography of the brain confirmed the presence of a left-sided occipitoparietal infarct. The non-invasive duplex Doppler study showed narrowing of the left common carotid artery with 90% stenosis of the left internal carotid artery. Aortography of the aortic arch confirmed these findings — apart from the severe left common carotid artery stenosis, the right brachiocephalic trunk and left subclavian artery origins appeared normal.

Exploration and endarterectomy of the patient's left common carotid artery 2 months after the stroke confirmed the presence of active peri-arterial inflammation. Six months after surgery the patient suddenly became blind in her left eye because of central retinal artery thrombosis, and the left common carotid artery was found to be occluded. The hemiparesis and motor dysphasia remained unchanged. The patient is now receiving sodium warfarin and prednisone 50 mg/kg/d.

Discussion

Takayasu's disease occurs mainly in females, with the age of onset ranging from 10 to 20 years.²⁻⁷ The disease is frequently characterized by constitutional symptoms and signs which include tiredness, headaches, fever, sweating, muscle weakness, nausea, blurred vision, weight loss, exertional dyspnoea, upper extremity claudication, absent upper extremity pulses, and elevated plasma protein levels and ESR.²⁻⁷ Some workers² refer to these manifestations as the acute inflammatory phase of the disease. Unfortunately, when they present most patients already have advanced arterial occlusion and evidence of collateral circulation because this is when they first develop symptoms, as in our cases.² At this stage, patients may also have cardiovascular and neurological signs of the disease.

The chronic arteriopathy of unknown origin gives rise to four complications — Takayasu's hypotensive ischaemic retinopathy, secondary hypertension, aortic regurgitation and aortic

or arterial aneurysm formation — some of which were present in cases 1 and 3.^{6,10} Coronary artery involvement is not a prominent feature of this disease. The outlook for the patient is determined by the presence or absence of complications and it has been pointed out that the prognosis for patients with single or multiple complications is poorer than that for patients with only mild complications or none.⁶ The natural course of the disease is chronic and is characterized by progressive deterioration and acute exacerbations.

The underlying lesion is a chronic arteritis of unknown aetiology causing narrowing of the vessel lumen, often combined with distal aneurysmal dilatation and secondary thrombus formation.^{4,11} It has been found that the arterial lesions are far more widespread than originally believed. It is now known that Takayasu's disease of the aorta may be confined to the arch or be extensive and involve the whole aorta and its branches, including the descending thoracic and abdominal aorta.⁴

Frequent laboratory findings in Takayasu's disease include hypochromic or normochromic normocytic anaemia; moderate leucocytosis; elevated ESR, α_2 -globulin and C-reactive proteins.⁴ Most studies report that the ESR is elevated during the early and active stages of the disease and gradually returns to normal after many years. The ESR has proved to be an excellent index of activity of the disease.^{5,7}

Recent findings suggest that there are genetically related factors in the disease and support auto-immunity as a cause. A recent study¹² from Japan shows a statistically significant frequency of A9 BW52 and BW52 DHO in haplotypes of these patients in contrast with healthy Japanese. Other workers have shown that patients with Takayasu's disease have defective T-lymphocyte function, increase in the IgG serum levels, and a reduction in serum complement components C3 and C4, suggesting that complement-binding immune complexes had been formed. Other findings, which include elevated ESR, antistreptolysin titres, positive C-reactive proteins and increased γ -globulin levels, support the theory that an auto-immune mechanism is responsible for the activation of the disease.¹²

The reported results of the treatment of Takayasu's disease have differed, probably because of the unpredictable systemic involvement.²⁻⁷ The course of the disease is usually progressive and fatal within a few years although some authors⁴ have reported a more favourable prognosis. Antibiotic treatment has had no effect while anticoagulants may prevent thrombosis formation or embolization. Despite treatment, the inflammatory process and the course of the disease may remain progressive. In many cases corticosteroid administration has resulted in remarkable clinical improvement. Steroid therapy has resulted in decreased ESR, normal temperature and relief of local pain overlying the arteries, and in some patients the radial pulse has reappeared. Not only are the patient's complaints ameliorated but progression of arterial involvement during the active period of the disease may be averted. It would appear that maintenance steroid therapy may lengthen the lifespan of these patients by causing remission of both systemic manifestations and those due to arterial insufficiency. The initial daily dose is usually 30 - 50 mg prednisone, more often the latter, gradually reduced to 10 - 7.5 mg/d. Some patients required steroid therapy for more than 4 years. As in our patients, the ESR is an excellent index both to disease activity and to favourable response to prednisone therapy. Occasionally steroids have had no effect on the disease, but usually they appear to be highly effective in the acute phase with little or no effect in chronic cases.²⁻⁷

Surgery has a limited but definite place in the treatment of Takayasu's disease.^{2,7,13} Generally, ischaemic signs in the upper extremities are not severe because of the development of adequate collateral circulation. Manifestations of numbness, sensation of cold, claudication, and Raynaud's phenomenon may occur. It has been suggested that occlusive lesions confined to the subclavian artery do not require surgical treatment. Surgical procedures which have been applied with success to relieve upper extremity ischaemia include subclavian-subclavian, axillo-axillary and femoro-axillary bypass using autogenous vein or Dacron grafts.³ Excision and graft replacement have been suggested for the treatment of aneurysms. In most series bypass or endarterectomy of the affected areas have had only limited success; the limitation has been attributed to suture failure, aneurysm formation or graft occlusion.⁶ Ishikawa⁶ stressed that in patients selected for surgery the markedly accelerated ESR should be normalized by steroid therapy before the operation.

Pregnancy and delivery may compound established cardiovascular complications and inflammatory activity of the disease. It has been stressed that close co-operation by the cardiologist, obstetrician and anaesthetist is mandatory during pregnancy, labour, delivery and the puerperium in the event of cardiac involvement in Takayasu's disease.¹⁰

Although the prognosis for most patients is fairly good, among the major factors causing death are congestive heart failure and cerebrovascular accidents; blindness is nearly always a serious complication.⁶

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